

In the claims:

Please amend the claims as follows:

Claims 1-8. (Canceled)

1/ 9. (Previously presented) An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1×10^{-10} M or less and a k_{off} rate constant of $1 \times 10^{-3} s^{-1}$ or less, as determined by surface plasmon resonance.

2/ 10. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} s^{-1}$ or less.

3/ 11. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} s^{-1}$ or less.

8 12. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less.

9 13. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

10/ 14. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

Claims 15-40. (Canceled)

16
41. (Original) An isolated human antibody, or an antigen-binding portion thereof, which

- a) inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-9}M$ or less;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

17 42. (Original) 16 The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 27; and a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 28.

18 43. (Original) 16 The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 29; and a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 30.

21 44. (Original) An isolated human antibody, or an antigen-binding portion thereof, having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 31, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 32.

22 45. (Original) 21 The isolated human antibody of claim 44, comprising a heavy chain constant region selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.

23 46. (Original) 22 The isolated human antibody of claim 45, wherein the antibody heavy chain constant region is IgG1.

24 47. (Original) 21 The isolated human antibody of claim 44, which is a Fab fragment.

25 48. (Original) 21 The isolated human antibody of claim 44, which is a F(ab')₂ fragment.

U.S.S.N. 09/534,717

4

Group Art Unit: 1647

26
49. (Original) The isolated human antibody of claim 44, which is a single chain Fv fragment. 21

Claims 50-87. (Canceled)

64-88. (Previously presented) A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim 9, 41, 44, 151, 153, 169, 167, 168, 172, 183, or 184, and a pharmaceutically acceptable carrier. 1121 27 29 41 44
45 48 50 51
Claims 89-90 (Canceled)

65-91. (Previously presented) The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of budesonide, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, mesalamine, olsalazine, balsalazide, antioxidants, antibodies to IL-1 receptor, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, pyridinyl-imidazole compounds, anti-TNF antibodies, or fragments thereof, and anti-LT antibodies. 14

Claims 92-141. (Canceled)

6-142. (Previously presented) The isolated human antibody, or antigen-binding portion thereof, of claim 9, which is a recombinant antibody, or antigen-binding portion thereof.

7-143. (Previously presented) The isolated human antibody of any one of claims 9 to 142, wherein the antibody is a neutralizing antibody. 1

11-144. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* phytohemagglutinin blast proliferation assay (PHA assay) with an IC₅₀ of 1 x 10⁻⁷ M or less. 7

U.S.S.N. 09/534,717

5

Group Art Unit: 1647

- 12 ~~145.~~ (Previously presented) The neutralizing antibody of claim ~~143~~, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-8} M or less
- 13 ~~146.~~ (Previously presented) The neutralizing antibody of claim ~~143~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC_{50} of 1×10^{-10} M or less.
- 14 ~~147.~~ (Previously presented) The neutralizing antibody of claim ~~143~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC_{50} of 1×10^{-11} M or less.
- 15 ~~148.~~ (Previously presented) The neutralizing antibody of claim ~~143~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC_{50} of 5×10^{-12} M or less.
- 19 ~~149.~~ (Previously presented) ~~16~~ The isolated human antibody, or antigen-binding portion thereof, of claim ~~41~~, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.
- 20 ~~150.~~ (Previously presented) ~~16~~ The isolated human antibody, or antigen-binding portion thereof, of claim ~~41~~, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.
- 27 ~~151.~~ (Previously presented) An isolated human antibody, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K_d of 1×10^{-10} M or less and binds to an epitope on the p40 subunit of human IL-12.
- 28 ~~152.~~ (Previously presented) ~~27~~ The isolated human antibody of claim ~~151~~, which neutralizes the activity of human IL-12.
- 29 ~~153.~~ (Currently amended) A neutralizing isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-2} s^{-1}$ ~~$1 \times 10^{-3} s^{-1}$~~ or less, as determined by surface plasmon resonance.

U.S.S.N. 09/534,717

6

Group Art Unit: 1647

30 ~~154~~. (Currently amended) The neutralizing isolated human antibody of claim ~~153~~, or an antigen-binding portion thereof, which dissociates from human IL-12 with a ~~29~~ k_{off} rate constant of $1 \times 10^{-4} s^{-1}$ or less.

31 ~~155~~. (Previously presented) The neutralizing isolated human antibody of claim ~~153~~, ~~29~~ or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} s^{-1}$ or less.

33 ~~156~~. (Currently amended) The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-7} M$ or less.

34 ~~157~~. (Currently amended) The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-8} M$ or less.

35 ~~158~~. (Currently amended) ~~32~~ The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-9} M$ or less.

36 ~~159~~. (Currently amended) ~~32~~ The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-10} M$ or less.

37 ~~160~~. (Currently amended) ~~32~~ The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-11} M$ or less.

38
161. (Currently amended) 32 The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-10} M or less.

39
162. (Currently amended) 32 The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-11} M or less.

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163. (Currently amended) 32 The neutralizing isolated human antibody of any one of claims ~~153~~ to ~~155~~ and ~~207~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 5×10^{-12} M or less.

41
164. (Previously presented) An isolated human antibody, or an antigen-binding portion thereof, which
a) dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-3} s^{-1}$ or less, as determined by surface plasmon resonance;
b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

42
165. (Previously presented) 41 The isolated human antibody of claim ~~164~~, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} s^{-1}$ or less.

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166. (Previously presented) 41 The isolated human antibody of claim ~~164~~, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} s^{-1}$ or less.

44
167. (Previously presented) An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and comprises:
a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and
a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

U.S.S.N. 09/534,717

8

Group Art Unit: 1647

~~168~~ ⁴⁵ (Previously presented) An isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26, and with a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

~~169~~ ⁴⁶ (Previously presented) ⁴⁵ The isolated human antibody, or an antigen-binding portion thereof, of claim ~~168~~, wherein the LCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 28 and the HCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 27.

~~170~~ ⁴⁷ (Previously presented) ⁴⁶ The isolated human antibody, or an antigen-binding portion thereof, of claim ~~169~~, wherein the LCVR further has a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 30 and the HCVR has a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 29.

~~171~~ ⁶⁹ (Previously presented) A pharmaceutical composition comprising an antibody or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody comprises:
a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and
a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

~~172~~ ⁴⁸ (Previously presented) An isolated human antibody that binds human IL-12 and is the antibody J695, or an antigen binding portion thereof.

~~173~~ ⁴⁹ (Previously presented) ⁴⁸ A pharmaceutical composition comprising the isolated human antibody of claim ~~172~~ and a pharmaceutically acceptable carrier.

Claims 174-182. (Canceled)

U.S.S.N. 09/534,717

9

Group Art Unit: 1647

50
183. (Previously presented) An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1.34×10^{-10} M or less, and neutralizes human IL-12.

51 184. (Previously presented) The isolated human antibody of claim 183, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K_d of 9.74×10^{-11} M or less.

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185. (Previously presented) The isolated human antibody, or antigen-binding portion thereof, of claims 183 or 184, which is a recombinant antibody, or antigen-binding portion thereof.

53 186. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-7} M or less.

54 187. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-8} M or less.

55 188. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less.

56 189. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

57 190. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

U.S.S.N. 09/534,717

10

Group Art Unit: 1647

58

~~191.~~ (Previously presented) The isolated human antibody of claim ~~185~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-10} M or less.

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~~192.~~ (Previously presented) The isolated human antibody of claim ~~185~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-11} M or less.

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~~193.~~ (Previously presented) The isolated human antibody of claim ~~185~~, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 5×10^{-12} M or less.

61

~~194.~~ (Previously presented) The isolated human antibody of claim ~~185~~, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC₅₀ of 1×10^{-9} M or less.

62

~~195.~~ (Previously presented) The isolated human antibody of claim ~~185~~, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC₅₀ of 1×10^{-10} M or less.

63

~~196.~~ (Previously presented) The isolated human antibody of claim ~~185~~, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC₅₀ of 1×10^{-11} M or less.

64

~~197.~~ (Previously presented) The pharmaceutical composition of claim ~~88~~, further comprising an additional therapeutic agent selected from the group consisting of anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, and anti-CD90 antibodies.

67 198. (Previously presented) The pharmaceutical composition of claim 88, 64
further comprising an additional therapeutic agent selected from the group consisting of
methotrexate, FK506, rapamycin, mycophenolate mofetil, leflunomide, non-steroidal
anti-inflammatory drugs (NSAIDs), ibuprofen, prednisolone, 6-mercaptopurines, soluble
p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13,
antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, TGF β , Vx740, anti-P7s, p-selectin
glycoprotein ligand (PSGL), p75TNFRlgG (EnbrelTM), p55TNFRlgG (LenerceptTM),
pyridinyl-imidazole compounds, anti-gp39 antibodies, anti-CD40L antibodies,
methotrexate, cytokine suppressive anti-inflammatory drugs (CSAIDs), leflunomide, MP,
mesalazine, chloroquinine/hydroxychloroquine, pencillamine, aurothiomalate, cochlincine,
salbutamol, terbutaline, salmeteral, theophylline, aminophylline, cromoglycate,
nedocromil, ketotifen, ipratropium, and oxitropium.

68 199. (Previously presented) The pharmaceutical composition of claim 88, 64
further comprising an additional therapeutic agent selected from the group consisting of
anti-IRAK antibodies, anti-NIK antibodies, anti-IKK antibodies, anti-p38 antibodies,
D2E7, cA2 (RemicadeTM), CDP 571, 5-aminosalicylic acid, TNFR-Ig constructs,
dexamethasone, aminosalicic acid, IL-1ra, methylprednisolone, cyclophosphamide,
methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a (AvonexTM), interferon- β 1b
(BetaseronTM), Copolymer 1 (Cop-1; CopaxoneTM), hyperbaric oxygen, clabribine, anti-
EMAP-II antibodies, IFN β 1a, IFN β 1b, and IL-1.

70 200. ((Previously presented) A pharmaceutical composition comprising the
antibody or an antigen binding portion thereof of claim 143, and a pharmaceutically
acceptable carrier. 7

71 201. (Previously presented) The pharmaceutical composition of claim 200, 70
further comprising an additional therapeutic agent selected from the group consisting of
budenoside, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-
mercaptopurine, azathioprine, metronidazole, mesalamine, olsalazine, balsalazide,
antioxidants, antibodies to IL-1 receptor, anti-IL-1 β monoclonal antibodies, anti-IL-6

U.S.S.N. 09/534,717

12

Group Art Unit: 1647

monoclonal antibodies, pyridinyl-imidazole compounds, anti-TNF antibodies, or fragments thereof, and anti-LT antibodies.

72 202. (Previously presented) The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, and anti-CD90 antibodies.

73 203. (Previously presented) The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of methotrexate, FK506, rapamycin, mycophenolate mofetil, leflunomide, non-steroidal anti-inflammatory drugs (NSAIDs), ibuprofen, prednisolone, 6-mercaptopurines, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, TGF β , Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), p75TNFRlgG (EnbrelTM), p55TNFRlgG (LenerceptTM), pyridinyl-imidazole compounds, anti-gp39 antibodies, anti-CD40L antibodies, methotrexate, cytokine suppressive anti-inflammatory drugs (CSAIDs), leflunomide, MP, mesalazine, chloroquine/hydroxychloroquine, pencillamine, aurothiomalate, cochlaine, salbutamol, terbutaline, salmeterol, theophylline, aminophylline, cromoglycate, nedocromil, ketotifen, ipratropium, and oxitropium.

74 204. (Previously presented) The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of anti-IRAK antibodies, anti-NIK antibodies, anti-IKK antibodies, anti-p38 antibodies, D2E7, cA2 (RemicadeTM), CDP 571, 5-aminosalicylic acid, TNFR-Ig constructs, dexamethasone, aminosalicylic acid, IL-1ra, methylprednisolone, cyclophosphamide, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a (AvonexTM), interferon- β 1b

U.S.S.N. 09/534,717

13

Group Art Unit: 1647

(BetaseronTM), Copolymer 1 (Cop-1; CopaxoneTM), hyperbaric oxygen, clabribine, anti-EMAP-II antibodies, IFN β 1a, IFN β 1b, and IL-1.

4 205. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1.34×10^{-10} M or less.

5 206. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 9.74×10^{-11} M or less.

32 207. (New) The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less.